DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

MAR 31 2000

The Honorable Thomas J. Bliley, Jr.
Chairman
Committee on Commerce
House of Representatives
Washington, D.C. 20515-6115

Dear Mr. Chairman:

Thank you for your continued interest in the regulatory status of silicone breast implants. This is in response to your letter of March 17, 2000, requesting documents and information pertaining to the Food and Drug Administration's (FDA or the Agency) decision to bring to Advisory Panel review a premarket approval application (PMA) for a saline-filled breast implant from a manufacturer that was currently being investigated by FDA's Office of Criminal Investigations (OCI). The PMA in question received an approval recommendation by the Advisory Panel.

It is not unusual for FDA to continue the panel review process when a sponsor is the subject of an ongoing investigation. There are a number of reasons for this policy. As your letter correctly notes, the existence of an investigation does not establish that improprieties or misconduct have occurred. If the Agency were routinely to halt application reviews while allegations were investigated and evaluated, the premarket review process would be significantly delayed. In addition, it is often the case that the nature of the allegations would not affect the review of the Advisory Panel, even if they were demonstrated to be true. Manufacturing issues, for example, might be the subject of an investigation and certainly could delay or prevent eventual approval of the product. The Advisory Panel, however, would not be asked to consider such information. Furthermore, allegations that may form the basis of a criminal investigation of a manufacturer may not reflect upon the safety or effectiveness of the product manufactured. For example, a criminal investigation that relates to false charges for investigational products would not reflect upon the safety and effectiveness of that product.

Most importantly, an Advisory Panel approval recommendation is simply that, a recommendation and the Agency is not bound to act on that recommendation. If information discovered or established following the meeting of the Advisory Panel gives the Agency reason to question the validity of the data the Panel reviewed, the Agency would not approve the application without additional deliberations. This is true whether questions about the validity of the data are raised by proof of criminal conduct or subsequent analyses that show inadvertent error.

The Agency's actions in this particular instance are also consistent with the stated policies of the Center for Devices and Radiological Health (CDRH). On May 29, 1991, CDRH issued a memo entitled, "Integrity of Data and Information Submitted to ODE" (I91-2) (copy enclosed). This memo describes the actions to be taken when there are questions about the reliability of data contained in an application. It states clearly that, "A submission that is referred . . . for verification of the data will not be cleared until the integrity of the data is established." It further states, "In the interim, the submission will be dealt with in accordance with established review procedures." Therefore, taking the PMA in question to the panel while there was an ongoing criminal investigation of the manufacturer was consistent with CDRH policy.

We would also like to point out that the time frames surrounding the review of a preamendments Class III device raise particular issues related to timely review. On August 19, 1999, FDA issued a final rule requiring the filing of a PMA or notice of a completion of a Product Development Protocol (PDP) for the silicone inflatable breast prosthesis, a currently-marketed, preamendments device. A PMA or notice of completion of a PDP for each implant was required to be filed on or before November 17, 1999. Any device for which a PMA or PDP was not filed by that date would be required to come off the market. The statute gives FDA 180 days to review and make a decision about those applications. If an approved PMA or completed PDP is not in effect for each such device on or before 180 days, the sponsor must immediately cease commercial distribution of the device. (The device may be distributed for investigational use if the requirements of the investigational device exemption regulations have been met.) In accordance with this process, FDA must complete its review of the PMA in question and render a decision by May 10, 2000. In the case of saline-filled breast implants, therefore, if

the Agency does not meet the timeframes specified in the final rule, the product would have to be withdrawn from the market. This would represent a significant disruption to the manufacturer and its customers, and needless anxiety to patients who may have to delay reconstruction procedures because the desired implant cannot be obtained. The Agency believes it is particularly important under these circumstances that allegations not hold up ongoing review.

Committee staff raised these concerns during a May 12, 1999, briefing on breast implants. At that time Committee staff were assured that FDA's OCI would inform CDRH if information uncovered during the investigation had implications for the safety of breast implants. We can assure you that that is still the case.

Regarding your request for documents relating to FDA's decision to proceed to the panel with the application from the manufacturer in question, the enclosed 1991 memo from CDRH is the only responsive document.

The Committee has requested that the Members be briefed on this issue. We are happy to provide such a briefing and will contact your staff to schedule.

In the interim, if you have further questions or concerns, please let us know.

Sincerely,

Melinda K. Plaisier
Associate Commissioner
for Legislation

Enclosure

cc: The Honorable John D. Dingell
Ranking Minority Member
Committee on Commerce

The Honorable Ron Klink
Ranking Minority Member
Subcommitte on Oversight
and Investigations
Committee on Commerce

Integrity of Data and Information Submitted to ODE May 29, 1991 (I91-2)

May 29, 1991

Integrity Memorandum #I91-2

Integrity of Data and Information Submitted to ODE

Purpose

The purpose of this Blue Book Memorandum is to specify the procedures to be followed by the ODE staff if there is a question concerning the integrity of data and information contained in any PMA, IDE or 510(K) submission. We want to encourage reviewers to be sensitive to the possibly of inaccurate, withheld or otherwise false data in submissions reviewed by ODE. For example, the data may appear to be fabricated or the device design may suggest that the performance data are not feasible.

Procedures

If a reviewer has any suspicion concerning the integrity of data or information provided to ODE in connection with any official submission, the matter should be raised through supervisory channels to the Division Director level. If the Division Director determines that it is necessary to verify the integrity of the data or information in the submission, the Division Director should notify the ODE Integrity Coordinator. The Integrity Coordinator will discuss the matter with the appropriate Program Operations Staff Manager and, if further action is indicated, the matter will be directed to the ODE/OCS Coordinator to initiate an inspection of the person or persons responsible for the submission of the questionable data or information. A submission that is referred to OCS for verification of the data will not be cleared until the integrity of the data is established.

During the interim, the submission will be dealt with in accordance with established review procedures.

The Integrity Coordinator will keep the Director, ODE, and the appropriate Division Directors informed of any inspections requested pursuant to these procedures.

Effective Date

These procedures are effective immediately.